

Amendments to the Claims

Claims 1-94 (cancelled)

95 (currently amended): An *in vitro* method of determining the effect of a substance on characteristics that are indicative of Alzheimer's Disease in rodent brain cells, said method comprising:

- (A) exposing said brain cells to a cathepsin D-increasing agent or compound under conditions that increase the concentration or amount of cathepsin D in said cells to an effective concentration,
- (B) maintaining said cells for a time that is sufficient to induce, relative to the levels present in the absence of said substance, one or more characteristics indicative of Alzheimer's Disease in said cells as a result of said increase in said cathepsin D,
- (C) adding said substance before, during and/or after said exposing or said maintaining; and
- (D) determining whether the presence of said substance has an effect on the induction of said one or more characteristics,

wherein said characteristics are selected from the group consisting of:

- (1) the formation of neurofibrillary tangles,
- (2) the hyperphosphorylation of tau,
- (3) the fragmentation of tau,
- (4) the production and/or release of brain-produced cytokines
TGF-beta, IL-1b, or TNF,
- (5) a microglia reaction or microglial activation,
- (6) indications of brain inflammatory reactions,

- (7) conversion of p35 to p25,
- (8) changes in the level and/or activity of cyclin dependent protein kinase 5 (cdk5), and
- (9) changes in the level and/or activity of mitogen activated protein kinases (MAPK),

wherein said effect on said induction increases or decreases of any or all of said characteristics in D(1)-D(9), and wherein the increase or decrease is indicative of the appearance or disappearance, respectively, of said characteristics of Alzheimer's Disease.

96 (previously added): The method of claim 95, wherein said characteristic is said formation of neurofibrillary tangles.

97 (previously amended): The method of claim 96, wherein said compound is selected from the group consisting of chloroquine, N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone, N-CBZ-L-phenylalanyl-L-phenylalanine-diazomethylketone, and beta-amyloid.

98 (previously amended): The method of claim 97, wherein said compound is N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone.

99 (previously added): The method of claim 96, wherein said brain cells are in the form of dissociated cells.

100 (previously added): The method of claim 96, wherein said brain cells are in the form of a brain slice.

101 (previously amended): The method of claim 100, wherein said brain slice is selected from the group consisting of a hippocampal slice, an entorhinal cortex slice, an entorhinohippocampal slice, a neocortex slice, a hypothalamic slice, and a cortex slice.

102 (cancelled)

103 (previously amended): The method of any one of claims 96-101, wherein said rodent brain cells are apolipoprotein E-deficient rodent brain cells.

104 (previously added): The method of claim 103, wherein said rodent is a mouse.

105 (previously added): The method of claim 103, wherein said rodent is a rat.

106 (previously amended): The method of any one of claims 96-101, wherein said rodent brain cells are apolipoprotein E4-containing rodent brain cells.

107 (previously added): The method of claim 106, wherein said rodent is a mouse.

108 (previously added): The method of claim 106, wherein said rodent is a rat.

109 (previously added): The method of claim 95, wherein said characteristic is said hyperphosphorylation of tau.

110 (previously amended): The method of claim 109, wherein said compound is selected from the group consisting of chloroquine, N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone, N-CBZ-L-phenylalanyl-L-phenylalanine-diazomethylketone, and beta-amyloid.

111 (previously amended): The method of claim 110, wherein said compound is N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone.

112 (currently amended): The method of claim 109, ~~where~~ wherein said brain cells are in the form of dissociated cells.

113 (previously added): The method of claim 109, wherein said brain cells are in the form of a brain slice.

114 (previously amended): The method of claim 113, wherein said brain slice is selected from the group consisting of a hippocampal slice, an entorhinal cortex slice, an entorhinohippocampal slice, a neocortex slice, a hypothalamic slice, and a cortex slice.

115 (cancelled)

116 (previously amended): The method of any one of claims 109-114, wherein said rodent brain cells are apolipoprotein E-deficient rodent brain cells.

117 (previously added): The method of claim 116, wherein said rodent is a mouse.

118 (previously added): The method of claim 116, wherein said rodent is a rat.

119 (previously amended): The method of any one of claims 109-114, wherein said rodent brain cells are apolipoprotein E4-containing rodent brain cells.

120 (previously added): The method of claim 119, wherein said rodent is a mouse.

121 (previously added): The method of claim 119, wherein said rodent is a rat.

122 (previously added): The method of claim 95, wherein said characteristic is said fragmentation of tau.

123 (previously amended): The method of claim 122, wherein said compound is selected from the group consisting of chloroquine, N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone, N-CBZ-L-phenylalanyl-L-phenylalanine-diazomethylketone, and beta-amyloid.

124 (previously amended): The method of claim 123, wherein said compound is N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone.

125 (currently amended): The method of claim 122, ~~where~~ wherein said brain cells are in the form of dissociated cells.

126 (previously added): The method of claim 122, wherein said brain cells are in the form of a brain slice.

127 (previously amended): The method of claim 126, wherein said brain slice is selected from the group consisting of a hippocampal slice, an entorhinal cortex slice, an entorhinohippocampal slice, a neocortex slice, a hypothalamic slice, and a cortex slice.

128 (cancelled)

129 (previously amended): The method of any one of claims 122-127, wherein said rodent brain cells are apolipoprotein E-deficient rodent brain cells.

130 (previously added): The method of claim 129, wherein said rodent is a mouse.

131 (previously added): The method of claim 129, wherein said rodent is a rat.

132 (previously amended): The method of any one of claims 122-127, wherein said rodent brain cells are apolipoprotein E4-containing rodent brain cells.

133 (previously added): The method of claim 132, wherein said rodent is a mouse.

134 (previously added): The method of claim 132, wherein said rodent is a rat.

135 (previously amended): The method of claim 95, wherein said characteristic is said production and/or release of brain-produced cytokines TGF-beta, IL-1b, or TNF.

136 (previously amended): The method of claim 135, wherein said compound is selected from the group consisting of chloroquine, N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone, N-CBZ-L-phenylalanyl-L-phenylalanine-diazomethylketone, and beta-amyloid.

137 (previously amended): The method of claim 136, wherein said compound is N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone.

138 (currently amended): The method of claim 135, ~~where~~ wherein said brain cells are in the form of dissociated cells.

139 (previously added): The method of claim 135, wherein said brain cells are in the form of a brain slice.

140 (previously amended): The method of claim 139, wherein said brain slice is selected from the group consisting of a hippocampal slice, an entorhinal cortex slice, an entorhinohippocampal slice, a neocortex slice, a hypothalamic slice, and a cortex slice.

141 (cancelled)

142 (previously amended): The method of any one of claims 109-114, wherein said rodent brain cells are apolipoprotein E4-deficient rodent brain cells.

143 (previously added): The method of claim 142, wherein said rodent is a mouse.

144 (previously added): The method of claim 142, wherein said rodent is a rat.

145 (previously amended): The method of any one of claims 135-140, wherein said rodent brain cells are apolipoprotein E4-containing rodent brain cells.

146 (previously added): The method of claim 145, wherein said rodent is a mouse.

147 (previously added): The method of claim 145, wherein said rodent is a rat.

148 (previously added): The method of claim 95, wherein said characteristic is said microglia reaction or microglial activation.

149 (previously amended): The method of claim 148, wherein said compound is selected from the group consisting of chloroquine, N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone, N-CBZ-L-phenylalanyl-L-phenylalanine-diazomethylketone, and beta-amyloid.

150 (previously amended): The method of claim 149, wherein said compound is N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone.

151 (currently amended): The method of claim 148, ~~where~~ wherein said brain cells are in the form of dissociated cells.

152 (previously added): The method of claim 148, wherein said brain cells are in the form of a brain slice.

153 (previously amended): The method of claim 152, wherein said brain slice is selected from the group consisting of a hippocampal slice, an entorhinal cortex slice, an entorhinohippocampal slice, a neocortex slice, a hypothalamic slice, and a cortex slice.

154 (cancelled)

155 (previously amended): The method of any one of claims 148-153, wherein said rodent brain cells are apolipoprotein E4-deficient rodent brain cells.

156 (previously added): The method of claim 155, wherein said rodent is a mouse.

157 (previously added): The method of claim 155, wherein said rodent is a rat.

158 (previously amended): The method of any one of claims 148-153, wherein said rodent brain cells are apolipoprotein E4-containing rodent brain cells.

159 (previously added): The method of claim 158, wherein said rodent is a mouse.

160 (previously added): The method of claim 158, wherein said rodent is a rat.

161 (previously added): The method of claim 95, wherein said characteristic is said indications of brain inflammatory reactions.

162 (previously amended): The method of claim 161, wherein said compound is selected from the group consisting of chloroquine, N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone, N-CBZ-L-phenylalanyl-L-phenylalanine-diazomethylketone, and beta-amyloid.

163 (previously amended): The method of claim 162, wherein said compound is N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone.

164 (currently amended): The method of claim ~~163~~ 161, ~~where~~ wherein said brain cells are in the form of dissociated cells.

165 (previously added): The method of claim 161, wherein said brain cells are in the form of a brain slice.

166 (previously amended): The method of claim 165, wherein said brain slice is selected from the group consisting of a hippocampal slice, an entorhinal cortex slice, an entorhinohippocampal slice, a neocortex slice, a hypothalamic slice, and a cortex slice.

167 (cancelled)

168 (previously amended): The method of any one of claims 161-166, wherein said rodent brain cells are apolipoprotein E4-deficient rodent brain cells.

169 (previously added): The method of claim 168, wherein said rodent is a mouse.

170 (previously added): The method of claim 168, wherein said rodent is a rat.

171 (previously amended): The method of any one of claims 161-166, wherein said rodent brain cells are apolipoprotein E4-containing rodent brain cells.

172 (previously added): The method of claim 171, wherein said rodent is a mouse.

173 (previously added): The method of claim 171, wherein said rodent is a rat.

174 (previously added): The method of claim 95, wherein said characteristic is said conversion of p35 to p25.

175 (previously amended): The method of claim 174, wherein said compound is selected from the group consisting of chloroquine, N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone, N-CBZ-L-phenylalanyl-L-phenylalanine-diazomethylketone, and beta-amyloid.

176 (previously amended): The method of claim 175, wherein said compound is N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone.

177 (currently amended): The method of claim 174, ~~where~~ wherein said brain cells are in the form of dissociated cells.

178 (previously added): The method of claim 174, wherein said brain cells are in the form of a brain slice.

179 (previously amended): The method of claim 178, wherein said brain slice is selected from the group consisting of a hippocampal slice, an entorhinal cortex slice, an entorhinohippocampal slice, a neocortex slice, a hypothalamic slice, and a cortex slice.

180 (cancelled)

181 (previously amended): The method of any one of claims 174-179, wherein said rodent brain cells are apolipoprotein E4-deficient rodent brain cells.

182 (previously added): The method of claim 181, wherein said rodent is a mouse.

183 (previously added): The method of claim 181, wherein said rodent is a rat.

184 (previously amended): The method of any one of claims 174-179, wherein said rodent brain cells are apolipoprotein E4-containing rodent brain cells.

185 (previously added): The method of claim 184, wherein said rodent is a mouse.

186 (previously added): The method of claim 184, wherein said rodent is a rat.

187 (previously added): The method of claim 95, wherein said characteristic is said changes in the level and/or activity of cyclin dependent protein kinase 5 (cdk5).

188 (previously amended): The method of claim 187, wherein said compound is selected from the group consisting of chloroquine, N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone, N-CBZ-L-phenylalanyl-L-phenylalanine-diazomethylketone, and beta-amyloid.

189 (previously amended): The method of claim 188, wherein said compound is N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone.

190 (currently amended): The method of claim 187, ~~where~~ wherein said brain cells are in the form of dissociated cells.

191 (previously added): The method of claim 187, wherein said brain cells are in the form of a brain slice.

192 (previously amended): The method of claim 191, wherein said brain slice is selected from the group consisting of a hippocampal slice, an entorhinal cortex slice, an entorhinohippocampal slice, a neocortex slice, a hypothalamic slice, and a cortex slice.

193 (cancelled)

194 (previously amended): The method of any one of claims 187-192, wherein said rodent brain cells are apolipoprotein E4-deficient rodent brain cells.

195 (previously added): The method of claim 194, wherein said rodent is a mouse.

196 (previously added): The method of claim 194, wherein said rodent is a rat.

197 (previously amended): The method of any one of claims 187-192, wherein said rodent brain cells are apolipoprotein E4-containing rodent brain cells.

198 (previously added): The method of claim 197, wherein said rodent is a mouse.

199 (previously added): The method of claim 197, wherein said rodent is a rat.

200 (previously added): The method of claim 95, wherein said characteristic is said changes in the level and/or activity of mitogen activated protein kinases.

201 (previously amended): The method of claim 200, wherein said compound is selected from the group consisting of chloroquine, N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone, N-CBZ-L-phenylalanyl-L-phenylalanine-diazomethylketone, and beta-amyloid.

202 (previously amended): The method of claim 201, wherein said compound is N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone.

203 (currently amended): The method of claim 200, ~~where~~ wherein said brain cells are in the form of dissociated cells.

204 (previously added): The method of claim 200, wherein said brain cells are in the form of a brain slice.

205 (previously amended): The method of claim 204, wherein said brain slice is selected from the group consisting of a hippocampal slice, an entorhinal cortex slice, an entorhinohippocampal slice, a neocortex slice, a hypothalamic slice, and a cortex slice.

206 (cancelled)

207 (previously amended): The method of any one of claims 200-205, wherein said rodent brain cells are apolipoprotein E4-deficient rodent brain cells.

208 (previously added): The method of claim 207, wherein said rodent is a mouse.

209 (previously added): The method of claim 207, wherein said rodent is a rat.

210 (previously amended): The method of any one of claims 200-205, wherein said rodent brain cells are apolipoprotein E4-containing rodent brain cells.

211 (previously added): The method of claim 210, wherein said rodent is a mouse.

212 (previously added): The method of claim 210, wherein said rodent is a rat.

213 (currently amended): An *in vitro* method of determining the effect of a substance on characteristics that are indicative of Alzheimer's Disease in rodent brain cells, said method comprising:

- (A) exposing said brain cells to a condition that disrupts lysosomal activity in said cells, wherein said condition comprises contacting said cells with a compound that disrupts lysosomal activity,
- (B) maintaining said cells for a time that is sufficient to induce, relative to the levels present in the absence of said substance, one or more characteristics indicative of said Alzheimer's Disease in said cells as a result of said disruption of said lysosomal activity,
- (C) adding said substance before, during and/or after said exposing or said maintaining; and
- (D) determining whether the presence of said substance has an effect on the induction of said one or more characteristics,

wherein said characteristics are selected from the group consisting of:

- (1) the formation of neurofibrillary tangles,
- (2) the hyperphosphorylation of tau,
- (3) the fragmentation of tau,
- (4) the production and/or release of brain-produced cytokines
TGF-beta, IL-1b, or TNF,
- (5) a microglia reaction or microglial activation,
- (6) indications of brain inflammatory reactions,
~~conversion of p35 to p25,~~
- (7) conversion of p35 to p25,
- (8) changes in the level and/or activity of cyclin dependent protein
kinase 5 (cdk5), and
- (9) changes in the level and/or activity of mitogen activated protein
kinases (MAPK),

wherein said effect on said induction increases or decreases ~~of~~ any or all of said characteristics in D(1)-D(9), and wherein the increase or decrease is indicative of the appearance or disappearance, respectively, of said characteristics of Alzheimer's Disease.

214 (previously added): The method of claim 213, wherein said characteristic is said formation of neurofibrillary tangles.

215 (previously amended): The method of claim 214, wherein said compound is selected from the group consisting of chloroquine, N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone, N-CBZ-L-phenylalanyl-L-phenylalanine-diazomethylketone, and beta-amyloid.

216 (previously added): The method of claim 215, wherein said compound is N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone.

217 (currently amended): The method of claim 214, ~~where~~ wherein said brain cells are in the form of dissociated cells.

218 (previously added): The method of claim 214, wherein said brain cells are in the form of a brain slice.

219 (previously amended): The method of claim 218, wherein said brain slice is selected from the group consisting of a hippocampal slice, an entorhinal cortex slice, an entorhinohippocampal slice, a neocortex slice, a hypothalamic slice, and a cortex slice.

220 (cancelled)

221 (previously amended): The method of any one of claims 214-219, wherein said rodent brain cells are apolipoprotein E4-deficient rodent brain cells.

222 (previously added): The method of claim 221, wherein said rodent is a mouse.

223 (currently amended): The method of claim ~~222~~ 221, wherein said rodent is a rat.

224 (previously amended): The method of any one of claims 214-219, wherein said rodent brain cells are apolipoprotein E4-containing rodent brain cells.

225 (previously added): The method of claim 224, wherein said rodent is a mouse.

226 (previously added): The method of claim 224, wherein said rodent is a rat.

227 (previously added): The method of claim 213, wherein said characteristic is said hyperphosphorylation of tau.

228 (previously amended): The method of claim 227, wherein said compound is selected from the group consisting of chloroquine, N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone, N-CBZ-L-phenylalanyl-L-phenylalanine-diazomethylketone, and beta-amyloid.

229 (previously amended): The method of claim 228, wherein said compound is N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone.

230 (currently amended): The method of claim 227, ~~where~~ wherein said brain cells are in the form of dissociated cells.

231 (previously added): The method of claim 227, wherein said brain cells are in the form of a brain slice.

232 (previously amended): The method of claim 231, wherein said brain slice is selected from the group consisting of a hippocampal slice, an entorhinal cortex slice, an entorhinohippocampal slice, a neocortex slice, a hypothalamic slice, and a cortex slice.

233 (cancelled)

234 (previously amended): The method of any one of claims 227-232, wherein said rodent brain cells are apolipoprotein E4-deficient rodent brain cells.

235 (previously added): The method of claim 234, wherein said rodent is a mouse.

236 (previously added): The method of claim 234, wherein said rodent is a rat.

237 (previously amended): The method of any one of claims 227-232, wherein said rodent brain cells are apolipoprotein E4-containing rodent brain cells.

238 (previously added): The method of claim 237, wherein said rodent is a mouse.

239 (previously added): The method of claim 237, wherein said rodent is a rat.

240 (previously added): The method of claim 213, wherein said characteristic is said fragmentation of tau.

241 (previously amended): The method of claim 240, wherein said compound is selected from the group consisting of chloroquine, N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone, N-CBZ-L-phenylalanyl-L-phenylalanine-diazomethylketone, and beta-amyloid.

242 (previously amended): The method of claim 241, wherein said compound is N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone.

243 (currently amended): The method of claim 240, ~~where~~ wherein said brain cells are in the form of dissociated cells.

244 (previously added): The method of claim 240, wherein said brain cells are in the form of a brain slice.

245 (previously amended): The method of claim 244, wherein said brain slice is selected from the group consisting of a hippocampal slice, an entorhinal cortex slice, an entorhinohippocampal slice, a neocortex slice, a hypothalamic slice, and a cortex slice.

246 (cancelled)

247 (previously amended): The method of any one of claims 240-245, wherein said rodent brain cells are apolipoprotein E4-deficient rodent brain cells.

248 (previously added): The method of claim 247, wherein said rodent is a mouse.

249 (previously added): The method of claim 247, wherein said rodent is a rat.

250 (previously amended): The method of any one of claims 240-245, wherein said rodent brain cells are apolipoprotein E4-containing rodent brain cells.

251 (previously added): The method of claim 250, wherein said rodent is a mouse.

252 (previously added): The method of claim 250, wherein said rodent is a rat.

253 (previously amended): The method of claim 213, wherein said characteristic is said production and/or release of brain-produced cytokines TGF-beta, IL-1b, or TNF.

254 (previously amended): The method of claim 253, wherein said compound is selected from the group consisting of chloroquine, N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone, N-CBZ-L-phenylalanyl-L-phenylalanine-diazomethylketone, and beta-amyloid.

255 (previously amended): The method of claim 254, wherein said compound is N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone.

256 (currently amended): The method of claim 253, ~~where~~ wherein said brain cells are in the form of dissociated cells.

257 (previously added): The method of claim 253, wherein said brain cells are in the form of a brain slice.

258 (previously amended): The method of claim 257, wherein said brain slice is selected from the group consisting of a hippocampal slice, an entorhinal cortex slice, an entorhinohippocampal slice, a neocortex slice, a hypothalamic slice, and a cortex slice.

259 (cancelled)

260 (previously amended): The method of any one of claims 253-258, wherein said rodent brain cells are apolipoprotein E4-deficient rodent brain cells.

261 (previously added): The method of claim 260, wherein said rodent is a mouse.

262 (previously added): The method of claim 260, wherein said rodent is a rat.

263 (previously amended): The method of any one of claims 253-258, wherein said rodent brain cells are apolipoprotein E4-containing rodent brain cells.

264 (previously added): The method of claim 263, wherein said rodent is a mouse.

265 (previously added): The method of claim 263, wherein said rodent is a rat.

266 (previously added): The method of claim 213, wherein said characteristic is said microglia reaction or microglial activation.

267 (previously amended): The method of claim 266, wherein said compound is selected from the group consisting of chloroquine, N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone, N-CBZ-L-phenylalanyl-L-phenylalanine-diazomethylketone, and beta-amyloid.

268 (previously amended): The method of claim 267, wherein said compound is N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone.

269 (previously added): The method of claim 266, wherein said brain cells are in the form of dissociated cells.

270 (previously added): The method of claim 266, wherein said brain cells are in the form of a brain slice.

271 (previously amended): The method of claim 270, wherein said brain slice is selected from the group consisting of a hippocampal slice, an entorhinal cortex slice, an entorhinohippocampal slice, a neocortex slice, a hypothalamic slice, and a cortex slice.

272 (cancelled)

273 (previously amended): The method of any one of claims 266-271, wherein said rodent brain cells are apolipoprotein E4-deficient rodent brain cells.

274 (previously added): The method of claim 273, wherein said rodent is a mouse.

275 (previously added): The method of claim 273, wherein said rodent is a rat.

276 (previously amended): The method of any one of claims 266-271, wherein said rodent brain cells are apolipoprotein E4-containing rodent brain cells.

277 (previously added): The method of claim 276, wherein said rodent is a mouse.

278 (previously added): The method of claim 276, wherein said rodent is a rat.

279 (previously added): The method of claim 213, wherein said characteristic is said indications of brain inflammatory reactions.

280 (previously amended): The method of claim 279, wherein said compound is selected from the group consisting of chloroquine, N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone, N-CBZ-L-phenylalanyl-L-phenylalanine-diazomethylketone, and beta-amyloid.

281 (previously amended): The method of claim 280, wherein said compound is N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone.

282 (currently amended): The method of claim 279, ~~where~~ wherein said brain cells are in the form of dissociated cells.

283 (previously added): The method of claim 279, wherein said brain cells are in the form of a brain slice.

284 (previously amended): The method of claim 283, wherein said brain slice is selected from the group consisting of a hippocampal slice, an entorhinal cortex slice, an entorhinohippocampal slice, a neocortex slice, a hypothalamic slice, and a cortex slice.

285 (cancelled)

286 (previously amended): The method of any one of claims 279-284, wherein said rodent brain cells are apolipoprotein E4-deficient rodent brain cells.

287 (previously added): The method of claim 286, wherein said rodent is a mouse.

288 (previously added): The method of claim 286, wherein said rodent is a rat.

289 (previously amended): The method of any one of claims 279-284, wherein said rodent brain cells are apolipoprotein E4-containing rodent brain cells.

290 (previously added): The method of claim 289, wherein said rodent is a mouse.

291 (previously added): The method of claim 289, wherein said rodent is a rat.

292 (previously added): The method of claim 213, wherein said characteristic is said conversion of p35 to p25.

293 (previously amended): The method of claim 292, wherein said compound is selected from the group consisting of chloroquine, N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone, N-CBZ-L-phenylalanyl-L-phenylalanine-diazomethylketone, and beta-amyloid.

294 (previously amended): The method of claim 293, wherein said compound is N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone.

295 (currently amended): The method of claim 292, ~~where~~ wherein said brain cells are in the form of dissociated cells.

296 (currently amended): The method of claim ~~294~~ 292, wherein said brain cells are in the form of a brain slice.

297 (previously amended): The method of claim 296, wherein said brain slice is selected from the group consisting of a hippocampal slice, an entorhinal cortex slice, an entorhinohippocampal slice, a neocortex slice, a hypothalamic slice, and a cortex slice.

298 (cancelled)

299 (previously amended): The method of any one of claims 292-297, wherein said rodent brain cells are apolipoprotein E4-deficient rodent brain cells.

300 (previously added): The method of claim 299, wherein said rodent is a mouse.

301 (previously added): The method of claim 299, wherein said rodent is a rat.

302 (previously amended): The method of any one of claims 292-297, wherein said rodent brain cells are apolipoprotein E4-containing rodent brain cells.

303 (previously added): The method of claim 302, wherein said rodent is a mouse.

304 (previously added): The method of claim 302, wherein said rodent is a rat.

305 (currently amended): The method of claim 213, wherein said characteristic is said changes in the level and/or activity of cyclin dependent protein kinase 5 (~~cdc5~~) (cdk5).

306 (previously amended): The method of claim 305, wherein said compound is selected from the group consisting of chloroquine, N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone, N-CBZ-L-phenylalanyl-L-phenylalanine-diazomethylketone, and beta-amyloid.

307 (previously amended): The method of claim 306, wherein said compound is N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone.

308 (currently amended): The method of claim 305, ~~where~~ wherein said brain cells are in the form of dissociated cells.

309 (previously added): The method of claim 305, wherein said brain cells are in the form of a brain slice.

310 (previously amended): The method of claim 309, wherein said brain slice is selected from the group consisting of a hippocampal slice, an entorhinal cortex slice, an entorhinohippocampal slice, a neocortex slice, a hypothalamic slice, and a cortex slice.

311 (cancelled)

312 (previously amended): The method of any one of claims 305-310, wherein said rodent brain cells are apolipoprotein E4-deficient rodent brain cells.

313 (previously added): The method of claim 312, wherein said rodent is a mouse.

314 (previously added): The method of claim 312, wherein said rodent is a rat.

315 (previously amended): The method of any one of claims 305-310, wherein said rodent brain cells are apolipoprotein E4-containing rodent brain cells.

316 (previously added): The method of claim 315, wherein said rodent is a mouse.

317 (previously added): The method of claim 315, wherein said rodent is a rat.

318 (previously added): The method of claim 213, wherein said characteristic is said changes in the level and/or activity of mitogen activated protein kinases.

319 (previously amended): The method of claim 318, wherein said compound is selected from the group consisting of chloroquine, N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone, N-CBZ-L-phenylalanyl-L-phenylalanine-diazomethylketone, and beta-amyloid.

320 (previously amended): The method of claim 319, wherein said compound is N-CBZ-L-phenylalanyl-L-alanine-diazomethylketone.

321 (currently amended): The method of claim 318, ~~where~~ wherein said brain cells are in the form of dissociated cells.

322 (previously added): The method of claim 318, wherein said brain cells are in the form of a brain slice.

323 (previously amended): The method of claim 322, wherein said brain slice is selected from the group consisting of a hippocampal slice, an entorhinal cortex slice, an entorhinohippocampal slice, a neocortex slice, a hypothalamic slice, and a cortex slice.

324 (cancelled)

325 (previously amended): The method of any one of claims 318-323, wherein said rodent brain cells are apolipoprotein E4-deficient rodent brain cells.

326 (previously added): The method of claim 325, wherein said rodent is a mouse.

327 (previously added): The method of claim 325, wherein said rodent is a rat.

328 (previously amended): The method of any one of claims 318-323, wherein said rodent brain cells are apolipoprotein E4-containing rodent brain cells.

329 (previously added): The method of claim 328, wherein said rodent is a mouse.

330 (previously added): The method of claim 328, wherein said rodent is a rat.